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| EXAMINER | |
|---|---|
| SRIVASTAVA, KAILASH C | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1657 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 07/10/2009 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/541,182 | KAPLAN ET AL. | |
| | Examiner | Art Unit | |
| | Kailash C. Srivastava | 1657 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *24 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *12-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/27/06&09/04/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

# DETAILED ACTION

## General Informal Matters

1. Response and amendment filed 24 April 2009 in response to Office Action mailed 1 April 2009 is acknowledged and entered.

## Claims Status

2. Claims 40-59 have currently been cancelled.

3. Claims 1-39 are currently pending.

4. Claims 12-39 have currently been withdrawn.

5. Claims 1-11 are examined on merits.

## *Restriction/Election*

6. Election without traverse of Group I invention encompassing Claims 1-11 filed 24 April 2009 in response to the Office Action mailed 1 April 2009 is acknowledged and entered. Applicants are correct that a species election was not required for this Group in the Office Action mailed 1 April 2009. Since the election is made without traverse, the restriction requirement is deemed proper and is made FINAL.

Accordingly, Claims 12-39 are withdrawn from further consideration as being directed to a non-elected invention. See 37 C.F.R. §1.142(b) and M.P.E.P. §821.03.

7. Claims 1-11 are examined on merits.

## Priority

8. Claim for domestic priority under 35 U.S.C. § 119(e) to Provisional United States (i.e., U.S.) Application Serial Numbers 60/438,393 filed 07 January 2003 is acknowledged.

9. Claim for priority under 35 U.S.C. § 371 to PCT/US04/00255 filed 07 January 2004 is acknowledged.

**Information Disclosure Statement**

10. The Information Disclosure Statements (i.e., IDSs) filed 27 January 2006 and on 04 September 2008 are acknowledged, have been made of record, considered and duly initialed sheet 1 of the appropriate PTO form for the IDS filed 27 January 2006 and duly initialed sheet for the IDS filed 04 September 2008 are enclosed with the Office Action.

Please note, despite the certification that the foreign patent references (i.e., WO-01/154667and WO-01/80921) were enclosed with the filing of IDS filed 27 January 2006, copies of said references are absent in the electronic file wrapper of e-DAN. To expedite the prosecution, however, the Examiner obtained copies of said foreign references from the appropriate database and considered them. For applicants' benefit said copies are enclosed herewith and appropriately listed on the PTO-892.

11. The information disclosure statement filed 27 January 2006 is objected to because said IDS partially fails to comply with 37 C.F.R. §1.98(a)(2), which requires a legible copy of each publication, or that portion which caused it to be listed on PTO 1449 or equivalent. Despite the certification that the copies of foreign patent references (i.e., WO-01/154667and WO-01/80921) and of all the Non-Patent Literature (i.e., NPL) references listed on USPTO 1449 or equivalent were enclosed with the filing of IDS filed 27 January 2006, copies of said references are absent in the electronic file wrapper of e-DAN. Although Examiner has obtained the WO references and considered them, the IDS pertaining to NPL has been placed in the application file.

If Applicants want said references to be considered and made part of the prosecution, please provide in response to the instant Office Action, a legible copy of each and every NPL document clearly listed on a new PTO 1449 or equivalent form sheet with complete citation (i.e., author (s) name, year of publication, complete title of the article, complete name of then scientific Journal/Magazine, Volume and number or issue of publication and the pages on which said reference appears in said Journal/Magazine) according to the instructions on said PTO form.

**Objection to Specification**

12. The amended specification filed on 30 June 2005 and on 14 June 2008 respectively is objected to because of the following reasons:

- At line 1 of amendment filed 30 June 2005, the correct application number is missing. Please note that the correct Serial Number of your Non-Provisional Application (i.e., USSN) under prosecution at the United States Patent and Trademark Office (i.e., USPTO) is 10/541,182. Please ensure that the correct USSN (i.e., 10/541,182) for the instant Non-Provisional U.S.

  application is cited in all future correspondence with this Office; and

- At Line 1 of each of amended paragraphs 0118 and 0142 filed on 14 June 2008, the technical name for the silk worm is non-conformant to the pertinent art. The correct name should be *Bombyx mori*, not Bombyx Mori. Appropriate correction is required.

Please also check the entire specification, including the abstract, for consistency and conformance to the requirements under 35 U.S.C. §112, first paragraph. 35 U.S.C. §112, first paragraph, requires the specification to be written in "full, clear, concise, and exact terms." Please, also ensure that no new matter is added to the specification while making the appropriate corrections in order to bring the instant application in conformance with the requirements of 35 U.S. C. §112, first paragraph.

***Claim Rejections - 35 U.S.C. §102***

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> ***A person shall be entitled to a patent unless –***
>
> ***(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.***

14. Claims 1-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Tsukada et al., (1994. Preparation and Application of Porous Silk Fibroin Materials. Journal of Applied Polymer Science, Volume 54, Pages 507-514).

Claims 1-8 recite a composition comprising 3 dimensional silk fibroin having interconnected pores, wherein pore diameter ranges from 10-1000, compressive modulus in range of at least 100 kPa to at least 250 Kpa, porosity of 80% and said material additionally comprises an additive, wherein said additive is a biologically, or pharmaceutically active compound.

Tsukada et al., teach a porous silk fibroin material having interconnected pores (Figures 1, 3 and 6A-F), wherein mean pore diameter size is in range of 2.5 µm to 106 µm (Figures and 5 and Table1). Said porous material is incorporated with acetylsalicyclic acid (Page 513, Column 1, Lines 26-34 under the Figure 7; Page 513, Column 2, Lines 1-11 under the Figure 8 and Figure 8). Please note, the pore size diameter of 2.5 µm to 106 µm covers the instantly claimed range of pore size diameter, acetylsalicyclic acid is a pharmaceutically active compound, a drug and drugs are usually bioactive. Despite the fact that Tsukada et al., are silent regarding the compressive modulus and the porosity, Claims 1-6 are anticipated by the prior art reference, because said porosity and compressive modulus are inherent properties of the porous material, especially in the view of the fact that the prior art reference teaches silk fibroin materials having the interconnected pores and pore size in the range that Tsukada et al., teach.

Therefore, the reference is deemed to anticipate the cited claims.

***Claim Rejections - 35 U.S.C. § 103***

15. The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> ***(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.***

16. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR §1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. §103(c) and potential 35 U.S.C. § *102*(f) or (g) prior art under 35 U.S.C. § 103(a).

17. Claims 1-9 are rejected under 35 U.S.C. §103(a) as obvious over combined teachings from Tsukada et al., (1994. Preparation and Application of Porous Silk Fibroin Materials. Journal of Applied Polymer Science, Volume 54, Pages 507-514) in view of each of Li et al., (2002.Study on Porous Fibroin Materials:3. Influence of Repeated Freeze-Thawing on the Structure and Properties of Porous Silk Fibroin Materials, Polymer Adv. Technology, Volume 13, Pages 605-610) and Alcock et al (US Patent 5,736,188 A) and further in view of Elçin et al (1996. Controlled release of endothelial cell growth factor from chitosan-albumin microspheres for localized angiogenesis: in vitro and in vivo studies. Artificial Cells Blood Substitutes and Immobilization Biotechnology 1996 May; Volume 24 number 3, Pages 257-71).

Claims 1-9 recite a composition comprising 3 dimensional silk fibroin having interconnected pores, wherein pore diameter ranges from 10-1000 microns, compressive modulus in range of at least 100 kPa to at least 250 Kpa, porosity of 80% and said material additionally comprises an additive, wherein said additive is a biologically, or pharmaceutically active compound, wherein biologically active compound is a cell growth factor.

Regarding Claims 1-9, teachings from Tsukada et al., have been discussed *supra* in item 13. Tsukada et al., further teach, porous substrates are highly attractive for various biotechnological applications (Page 597, Column 2, Lines 39-43) and the properties of silk fibroin membranes can be improved by blending said membranes with natural polymers e.g., chitosan (Page 597, Column 1, Lines 35-39). Tsukada et al., are, however, silent regarding the biological active compound as the cell growth factor.

Li et al., citing art-known literature teach, "application of silk fibroin porous materials having pore size of 100-150 μm for cell culture substances and artificial skins (Page 605, Column 2, Line 32) and further teach utility of said materials as porous drug delivery carriers, cell culture matrices and artificial skins because of the suitability of said porous membranes for cell-proliferation (Page 606, Column 1, Lines 1-9).

Please note chitosan is an art-known cell growth enhancer because it releases endothelial cell growth factor (ECGF, See, Elçin et al., 1996, Abstract, Lines 1-4). Please note further, cell proliferation and skin repair would not take place unless the silk fibroin- chitosan based fibrous materials (e.g., artificial skins) did not have the cell growth factor-namely chitosan in it.

Alcock et al., teach porous materials comprising gelatin, silk fibroin, chitosan, collagen or combinations thereof, especially combination of gelatin, chitosan and silk fibroin and further teach said materials have average pore diameters of 60 μm (Column 11, Lines 55-67; Column 22, Lines 15-16).

One having ordinary skill in the art at the time the invention was made would have been motivated to modify/combine the teachings from Tsukada et al., with the beneficial teachings from Li et al., Elçin et al., and Alcock et al., to obtain a "composition comprising 3 dimensional silk fibroin having interconnected pores, wherein pore diameter ranges from 10-1000 microns, compressive modulus in range of at least 100 kPa to at least 250 Kpa, porosity of 80% and said material additionally comprises an additive, wherein said additive is a biologically, or pharmaceutically active compound, wherein biologically active compound is a cell growth factor"; because Li et al., teach application of silk fibroin porous materials having pore size of 100-150 μm for cell culture substances and artificial skins and further teach utility of said materials as porous drug delivery carriers, cell culture matrices and artificial skins because of the suitability of said porous membranes for cell-proliferation, Alcock et al., teach porous materials comprising gelatin, silk fibroin, chitosan, collagen or combinations thereof, especially combination of gelatin, chitosan and silk fibroin and Elçin et al., teach chitosan to be a cell growth factor, particularly of endothelial cells. The combined teachings from Tsukada et al., with the beneficial teachings from Li et al., Alcock et al., and Elçin et al., teach each of the elements claimed in currently presented Claims 1-9.

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify/combine the teachings from Tsukada et al., with the beneficial teachings from Li et al., Elçin et al., and Alcock et al., to obtain a composition comprising 3 dimensional silk fibroin having interconnected pores, wherein pore diameter ranges from 10-1000 microns, compressive modulus in range of at least 100 kPa to at least 250 Kpa, porosity of 80% and said material additionally comprises an additive, wherein said additive is a biologically, or pharmaceutically active compound, wherein biologically active compound is a cell growth factor because Li et al., teach application of silk fibroin porous materials having pore size of 100-150 μm for cell culture substances and artificial skins and further teach utility of said materials as porous drug delivery carriers, cell culture matrices and artificial skins because of the suitability of said porous membranes for cell-proliferation, Alcock et al., teach porous materials comprising gelatin, silk fibroin, chitosan, collagen or combinations thereof, especially combination of gelatin, chitosan and silk fibroin and Elçin et al., teach chitosan to be a cell growth factor, particularly of endothelial cells.

**Conclusion**

18. For aforementioned reasons, no Claims are allowed. Dependent claims 10-11 are not taught by the above references. A further search and/or consideration may be required for said Claims on the basis of the response filed to the instant office action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kailash C. Srivastava whose telephone number is (571) 272-0923. The examiner can normally be reached on Monday to Thursday from 7:30 A.M. to 6:00 P.M. (Eastern Standard or Daylight Savings Time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at (571)-272-0925 Monday through Thursday 7:30 A.M. to 6:00 P.M. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding may be obtained from the Patent Application Information Retrieval (i.e., PAIR) system. Status information for the published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (i.e., EBC) at: (866)-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kailash C Srivastava/
Examiner, Art Unit 1657

Kailash C. Srivastava
Patent Examiner
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04 July 2009

/Ralph Gitomer/

Primary Examiner, Art Unit 1657